



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/750,323	12/30/2003	Stefan M. Pulst	3350.1000-005	4927

21005 7590 04/17/2006

HAMILTON, BROOK, SMITH & REYNOLDS, P.C.
530 VIRGINIA ROAD
P.O. BOX 9133
CONCORD, MA 01742-9133

EXAMINER

GOLDBERG, JEANINE ANNE

ART UNIT PAPER NUMBER

1634

DATE MAILED: 04/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/750,323

Applicant(s)

PULST, STEFAN M.

Examiner

Jeanine A. Goldberg

Art Unit

1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 February 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-41 is/are pending in the application.
- 4a) Of the above claim(s) 1-26 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 27-41 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|----------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>09/04</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. This action is in response to the papers filed February 6, 2006.
2. Currently, claims 1-41 are pending. Claims 1-26 are withdrawn from consideration.
3. Claims 27-41 are examined on the merits.

Priority

4. The instant application claims priority to parent application , 09/083, 268 filed May 22, 1998 and 08/727,084 filed 10/8/96 and provisional applications filed 5/8/96 and 7/19/96.

It is noted that the first line of the specification does not contain an updated status of the applications. Appropriate correction is required.

The provisional filed 5/8/96 discloses a nucleic acid of approximately 310 nucleotides and the corresponding amino acid sequence. The specific primers, namely SEQ ID NO: 6 and 7 are disclosed in the provisional application (Figure 2). Moreover, as seen in Figure 3, SCA2 patients appear to have a band around 194 in addition to the band around 130. The provisional application specifically states that "on agarose electrophoresis, a single band of approximately 130 bp was detected in 20 normal individuals (page 36). Further, "in contrast all 15 patients with SCA2 from 3 independent families showed one allele in the normal size range and a larger allele ranging from approximately 200 to 220 bp" (page 37). This does not appear to support 35 CAG repeats. Specifically given a SCA2 patient has 200 bp and the normal has 130

bp, the difference is 70 base pairs. 70 base pairs with a 3 base pair repeat provides 23 additional repeats. Since Figure 2 provides the 130 bp region of the normal individuals contains 22 repeats, it follows that the SCA2 patients would have 45 repeats given the information in the specification. Alternatively if the SCA2 patient was assumed to have 220 bp, the SCA2 patient would appear to have 52 repeats. This does not support at 35 or more repeats.

The provisional filed 7/19/96 discloses a nucleic acid sequence of approximately 500 nucleotides and a cDNA sequence of approximately 4094 nucleotides and the corresponding predicted amino acids. The provisional application states that a "common allele of 22 repeats and a less frequent allele of 23 repeats were observed on normal chromosomes (page 42). Further, "in patients from three independent SCA2 pedigrees extended alleles ranging from 36-52 repeats were observed (page 42).

The parent application 08/727,084, filed 10/8/96 appears to be the first time a SCA2 gene was provided. Claims 44-47 are directed to a SCA2 gene which was not completed until the parent application.

The MPEP 706.02 states, "If the application is a continuation-in-part of an earlier U.S. application, any claims in the new application not supported by the specification and claims of the parent application have an effective filing date equal to the filing date of the new application. Any claims which are fully supported under 35 U.S.C. 112 by the earlier parent application have the effective filing date of that earlier parent application". In essence, one claim is entitled to one priority date. As outlined above, the instant claims are directed to embodiments which are entitled to different dates.

Thus, the claim has not been fully supported by the earliest date, therefore the later date is the effective filing date.

New Matter

5. Claims 30-38, 40 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In the amended claims 30, reference to "nucleotides 303 to 657 of SEQ ID NO: 2" and "723 to 890 of SEQ ID NO: 2" are included. The amendment proposes that the new claim language is supported on pages 20, 32, 33, 34, Example 3 and Figure 6a. The passage from page 20 is not directed to amplification primers and their binding regions. The passage on page 32 is not directed to primers. The passage on page 33 states using "primers that amplify at least a nucleic acid fragment of SEQ ID NO: 2 containing nucleotides 658-723 of SEQ ID NO: 2". This recitation within the specification, while provide support for amplifying using primers which would amplify the CAG repeat region, does not provide basis for the specific position of 303-657 and 723-890 of SEQ ID NO: 2. On page 34, lines 15-26, the specification teaches diagnostic nucleic acids are derived from SEQ ID NO: 2 (Figure 6), preferably derived from nucleotides 163-657 and nucleotides 724-4098, with primes SCA2-A and SCA2-B being especially preferred. While this passage supports primers which are upstream and downstream of the CAG repeat region, this does not provide support for the narrow genus of primer binding regions which are instantly claimed. At the time the invention

was made, based upon the specification, the applicant's do not appear to have contemplated that the narrow regions of 303-657 and 723-890 of SEQ ID NO: 2. The concept of "nucleotides 303 to 657 of SEQ ID NO: 2" and "723 to 890 of SEQ D NO: 2". does not appear to be part of the originally filed invention. Therefore, recitation "nucleotides 303 to 657 of SEQ ID NO: 2" and "723 to 890 of SEQ ID NO: 2" constitutes new matter.

With respect to Claim 31, the instant claims are drawn to diagnosing SCA2 normal individuals by determining a number of CAG repeats "between 15-24". The instant specification teaches "a normal amount of CAG repeats in the SCA2 gene (SEQ ID NO: 2) has been found to be about 22, while 23 CAG repeats is occasionally observed" (page 31, lines 5-7). While this passages supports normal individuals with 22 and 23 repeats, the specification has not contemplated that the lower bound for normal individuals is 15 and the upper bound is 24. Moreover, there is no indication in the specification that normal individuals may have 15, 16, 17, 18, 19, 20, 21 or 24 CAG repeats within the CAG repeat region of SEQ ID NO: 2. In fact, the specification states "the SCA2 repeat is highly unusual, because only two alleles are observed in the normal population. A common allele with 22 repeats is found on 92% of chromosomes, a rare second allele in 8% of chromosomes" (page 31, lines 28-30). Therefore, the specification specifically provides for 100% of the normal alleles as being either 22 or 23 repeats. The concept of "15-24 CAG repeats in said nucleic acid sample would be negative for spinocerebellar ataxia type 2" does not appear to be part of the originally

filed invention. Therefore, recitation "15-24 CAG repeats in said nucleic acid sample would be negative for spinocerebellar ataxia type 2" constitutes new matter.

With respect to Claims 32-33, the specification does not appear to support these regions of primer binding. On page 34, lines 15-26, the specification teaches diagnostic nucleic acids are derived from SEQ ID NO: 2 (Figure 6), preferably derived from nucleotides 163-657 and nucleotides 724-4098, with primes SCA2-A and SCA2-B being especially preferred. While this passage supports primers which are upstream and downstream of the CAG repeat region, this does not provide support for the narrow genus of primer binding regions which are instantly claimed. The specification has provided two specific examples of SCA2 primers, namely SCA2-A and SCA2-B. These primers are not located in the binding region instantly claimed. Therefore, the specification had not contemplated these two specific primers from the large genus of primers which were generically provided in the specification. Therefore, at the time the invention was made, the instant specification does not appear to have basis for a primer with a sequence complementary to nucleotides 637-656 of SEQ ID NO: 2 and 764-783 of SEQ ID NO: 2. It is noted that these primers were claimed by the party to which applicant wishes to provoke an interference, however, applicant does not have sufficient basis for copying such claims.

With respect to Claim 36, the amendments provides that a probe is used to measure the number of CAG repeats, wherein the probe has a sequence greater than 22 CAG repeats. The amendment teaches that support for the claim may be found on pages 20, 21, 22, 33 and Example 3 and 4. The recitation on page 20 does not provide

Art Unit: 1634

any support for a (CAG)22 probe. Page 20 does discuss probes, but the text does not provide any indication that the probe is a CAG repeat probe or that the probe contains more than 22 repeats. Pages 21-23 fail to discuss CAG probes. Example 3 teaches hybridizing PCR products with (CAG)10 probes (page 43, lines 33-34). The specification fails to provide any contemplation of a (CAG)22 probe for determining the number of CAG repeats. The concept of "a probe having a sequence greater than 22 CAG repeats" does not appear to be part of the originally filed invention. Therefore, recitation "a probe having a sequence greater than 22 CAG repeats" constitutes new matter.

Claim 40 is drawn to a method of diagnosing CAG repeats, however the specification does not appear to discuss 32 or more CAG repeats.

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 112-Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 27-29, 39, 41 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to the SCA2 gene and the CAG repeat region.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2b 1111, clearly states that “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the ‘written description’ inquiry, whatever is now claimed”. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. In *The Regents of the University of California v. Eli Lilly* (43 USPQ2b 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that “An adequate written description of a DNA...’ required a precise definition, such as by structure, formula, chemical name, or physical properties’, not a mere wish or plan for obtaining the claimed chemical invention”.

In analyzing whether the written description requirement is met for a genus claim, it is first determined whether a representative number of species have been described by their complete structure. The specification has described a single CAG repeat region which is associated with SCA2. However, the specification has not described more than one CAG repeat region associated with SCA2. SE QID NO: 2 comprises additional CAG repeat regions, for example at nucleotides 3726. There is substantial variability among the CAG repeat regions encompassed within the scope of the claims

because SEQ ID NO: 2 is only a fragment of chromosome 12q24.1 which contains several regions with multiple CAG repeats, i.e. a CAG repeat region. Weighing all factors, 1) partial structure of the DNA, 2) breadth of the claims as reading on CAG repeat regions yet to be discovered in 3) the lack of correlation between the structure and function of the genes; in view of the level of knowledge and skill in the art, one skilled in the art would not recognize from the disclosure that the applicant was in possession of the genus of CAG repeats from Chromosome 12q24.1. Accordingly, Applicants have not adequately disclosed the relevant identifying characteristics of a representative number of species within the claimed genus.

Accordingly, Applicants have not adequately disclosed the relevant identifying characteristics of a representative number of species within the claimed genus.

Claim Rejections - 35 USC § 112-Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 27-41 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for detecting the presence of a CAG repeat in SEQ ID NO: 2, does not reasonably provide enablement for a method of detecting the presence of a CAG repeat region in the SCA2 gene on human chromosome 12q24.1 in an individual or a method of diagnosing SCA2 in a human sample by identifying the presence of a CAG repeat in a nucleic acid sample from chromosome 12q24.1 wherein

the presence of a larger number of CAG repeats than exists in a normal population is indicative of SCA2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

“Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in *Ex parte Forman*. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.”

The nature of the invention and breadth of claims

The claims are broadly drawn to a method of detecting the presence of a CAG repeat region in the SCA2 gene on human chromosome 12q24.1 in an individual. The claims are also broadly drawn to a method of diagnosing SCA2 in a human sample by identifying the presence of a CAG repeat in a nucleic acid sample from chromosome 12q24.1 wherein the presence of a larger number of CAG repeats than exists in a normal population is indicative of SCA2.

The invention is in a class of invention which the CAFC has characterized as “the unpredictable arts such as chemistry and biology.” *Mycogen Plant Sci., Inc. v. Monsanto Co.*, 243 F.3d 1316, 1330 (Fed. Cir. 2001).

The unpredictability of the art and the state of the prior art

Trottier teaches using a monoclonal antibody that selectively recognizes polyglutamine expansion such that the intensity of signal depends on the length of the polyglutamine expansion, and the antibody also detect specific pathological proteins expected to contain such expansion, in SCA2 and in autosomal dominant cerebellar ataxia with retinal degeneration, whose genes have not yet been identified (abstract).

Filla provides that SCA2 has been assigned to chromosome 12q23-24.1. Filla teaches that previous studies of the SCA2 locus have found that onset is earlier in the offspring than in the parent in their SCA2 family. "Anticipation, which may also be due to observer artifact, suggests the presence of an expanded trinucleotide repeat in SCA2, as found in SCA1" (page 795, col 2).

Pulst et al. (herein referred to as Pulst) teaches linkage of SCA2 to 12q and established closer flanking markers for SCA2. Pulst teaches that "given the recent identification of an expanded CAG triplet repeat in SCA1, this finding suggests a similar mechanism may underlie at least some case of SCA2 as well" (pages 8, col 2).

Guidance in the Specification.

The specification fails to provide a specific definition of the SCA2 gene. The specification teaches "such nucleic acids can be obtained, for example, from human chromosome 12, specifically at the q24.1 locus, which is the site of mutations that cause SCA2" (page 10, lines 22-25). Moreover, the specification teaches "nucleic acids may include, but are not limited to, nucleic acids having substantially the same nucleotide sequence as nucleotides 163-4098 set forth in SEQ ID NO: 2" (page 11, lines 8-12). Thus, there is no specific teaching in the specification of the definition of SCA2 gene.

The guidance provided by the specification amounts to an invitation for the skilled artisan to try and follow the disclosed instructions to make and use the claimed invention.

Quantity of Experimentation

The quantity of experimentation in this area is extremely large since there is significant number of parameters which would have to be studied. The claims are drawn to detecting CAG repeats in 12q24.1 and/or the SCA2 gene, however the specification does not clearly define what is meant by the recitation "SCA2 gene". While the specification teaches [with respect to the 'SCA 2 gene'] "such nucleic acids can be obtained, for example, from human chromosome 12, specifically at the q24.1 locus, which is the site of mutations that cause SCA2" (page 10, lines 22-25), the q24.1 locus on chromosome 12 encompasses thousands of sequences, including sequences that would define the SCA2 gene such as regulatory sequences, introns, etc. that have not been taught or described in the specification. Practice of the method as broadly as it is claimed encompasses the use of a large number of unknown CAG repeat sequences that have not been taught in either the specification or the art. The incomplete disclosure of a "SCA2 gene" in the specification does not support the full scope of the claimed method. While the specification asserts that DNA probes derived from the SCA2 gene could be used to isolate a nucleic acid encoding an SCA2 polypeptide (p. 10, lines 30-35), the specification does not teach any probes derived from SCA2 genomic DNA nor does the specification teach the genomic DNA that the probes would be derived from. Further, the unclear definition of "SCA2 gene" does not support the full scope of the claimed method. It is unclear what genomic sequences the term "gene" encompasses, for instance is such limited to only intronic sequences, or does it include

5' and 3' noncoding sequences, regulatory regions, etc. As stated previously, these sequences have not been taught by the specification. Further, while the specification teaches with regard to sequences that would be included in the SCA 2 gene "nucleic acids may include, but are not limited to, nucleic acids having substantially the same nucleotide sequence set forth in SEQ ID NO: 2" (page 11, lines 8-12), the specification does not define what is meant by 'substantially the same nucleotide sequence as...' such that the skilled artisan would be able to determine whether such recitation encompassed only the degeneracy of the genetic code, or also encompassed nucleotide polymorphisms or mutations that have not been taught in the specification. Neither the specification nor the art teach the skilled artisan how to make or use the invention as broadly as it is claimed. Given the lack of a clear definition as to what is encompassed by the recitation of the "SCA2 gene", the skilled artisan would not be able to determine what constitutes the SCA2 gene on chromosome 12 and would be therefore be required to perform undue experimentation to practice the invention as broadly as it is claimed.

The claims are also drawn to detecting "CAG repeat in the SCA2 gene on human chromosome 12q24.1 wherein the presence of a larger number of CAG repeats than exists in a normal population is indicative of SCA2." As noted above, the SCA2 gene contains several CAG repeat regions which have not been taught to be associated with SCA2. Further, it is unclear what is encompassed within "normal" for each of these regions and whether these regions are predictably associated with disease. The ordinary artisan would be required to perform further unpredictable and undue experimentation to determine what the ranges for "normal" and "diseased" individuals encompasses and whether these regions are even associated with SCA2.

Therefore, undue and unpredictable experimentation would be required to determine whether an association between the CAG repeat region on 12q24.1 and SCA2. Given the unclear definition of "SCA2" as the claims are presently written, the mere detection of a larger number of CAG repeats than exists in a normal population on chromosome 12, is not indicative of SCA2.

This would require significant inventive effort, with each of the many intervening steps, upon effective reduction to practice, not providing any guarantee of success in the succeeding steps.

Level of Skill in the Art

The level of skill in the art is deemed to be high.

Conclusion

In the instant case, as discussed above, in a highly unpredictable art where the art fails to teach associations between diseases and mutations. Further, the prior art and the specification provides insufficient guidance. Thus given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that art, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, the absence of a working example and the negative teachings in the prior art balanced only against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one of skill in the art to perform the method of the claim as broadly written.

Claim Rejections - 35 USC § 112- Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 27-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 27-29 are indefinite over the recitation "the CAG" repeat region because "the CAG" repeat region lacks proper antecedent basis. Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 39 are rejected under 35 U.S.C. 102(a) as being anticipated by Trottier et al. (Nature, Vol. 378, pages 403-406, November 1995).

This rejection is based upon the interpretation that the claims do not require obtaining a nucleic acid sample. The claims encompass detecting the presence of a CAG repeat region in the SCA2 gene indirectly, namely using an antibody.

Trottier teaches using a monoclonal antibody that selectively recognizes polyglutamine expansion. The intensity of signal depends on the length of the polyglutamine expansion, and the antibody also detect specific pathological proteins expected to contain such expansion, in SCA2 and in autosomal dominant cerebellar ataxia with retinal degeneration, whose genes have not yet been identified (abstract). Trottier teaches that all patient, including the SCA2 patient showed the 150K protein, which was not detected in a normal relative (lane 9, 4, respectively). Trottier teaches that "by analogy with data obtained with mutated HDPs, these results suggest that the polyglutamine stretch contained in the 150K protein increases in size through parental transmission, giving a stronger signal, and account for the anticipation phenomenon observed in these families and in previous studies of SCA2 (page 404, col. 2). Therefore, Trottier has indirectly detected the presence of a CAG repeat region in the SCA2 gene on chromosome 12 in an individual using 1C2 antibody which selectively recognizes polyglutamine expansion.

10. Claims 27-35, 37-41 are rejected under 35 U.S.C. 102(g) as being anticipated by Tsuji et al (US Pat. 6,251,589, June 26, 2001).

It is noted that this rejection may be overcome by a submission under 37 CFR 608 (a) or 608 (b). In the event that applicant can provide such submission, the case would be recommended for interference.

Tsuji teaches a method for diagnosing spinocerebellar ataxia type 2 in a human nucleic acid sample comprising the steps of: amplifying said nucleic acid sample with a

Art Unit: 1634

first primer and a second primer by polymerase chain reaction wherein said first primer hybridizes to a region of SEQ ID NO: 1 and said second primer hybridizes to a region of SEQ ID NO: 3; obtaining an amplification product of said nucleic acid sample by said polymerase chain reaction; and measuring a number of CAG repeats in said amplification product, wherein a number of 35 or more CAG repeats in said nucleic acid sample is indicative of said spinocerebellar ataxia type 2 and a number of 15-24 CAG repeats in said nucleic acid sample would be negative for SCA2 (limitations of Claims 27-33, 37-41). Tsuji teaches specific techniques of measuring and analyzing the CAG repeats of the SCA2 gene, namely gel electrophoresis, sequencing, and using hybridization probes (Claims 4-6 of 6,251,589)(limitations of instant Claim 34-35).

Furthermore as provided in the working Example 2 of Tsuji, Tsuji teaches that in all of the normal genes, the numbers of the CAG repeat units were not more than 24, while in all of the SCA2 genes, they were not less than 35 (col. 6, lines 45-50)(limitations of Claims 55-56).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

11. Claims 27-29, 39, 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Trottier et al. (Nature, Vol. 378, pages 403-406, November 1995) in view of either

Filla (Neurology, Vol. 45, pages 793-796, April 1995) or Pulst et al. (Nature Genetics, Vol. 5, pages 8-10, 1993).

Trottier teaches using a monoclonal antibody that selectively recognizes polyglutamine expansion. The intensity of signal depends on the length of the polyglutamine expansion, and the antibody also detect specific pathological proteins expected to contain such expansion, in SCA2 and in autosomal dominant cerebellar ataxia with retinal degeneration, whose genes have not yet been identified (abstract). Trottier teaches that all patient, including the SCA2 patient showed the 150K protein, which was not detected in a normal relative (lane 9, 4, respectively). Trottier teaches that "by analogy with data obtained with mutated HDPs, these results suggest that the polyglutamine stretch contained in the 150K protein increases in size through parental transmission, giving a stronger signal, and account for the anticipation phenomenon observed in these families and in previous studies of SCA2 (page 404, col. 2). Therefore, Trottier has indirectly detected the presence of a CAG repeat region in the SCA2 gene on chromosome 12 in an individual using 1C2 antibody which selectively recognizes polyglutamine expansion.

Trottier does not specifically teach the position of "the SCA2 gene" as on chromosome 12q23-24.1.

However, Filla provides that SCA2 has been assigned to chromosome 12q23-24.1. Filla teaches that previous studies of the SCA2 locus have found that onset is earlier in the offspring than in the parent in their SCA2 family. "Anticipation, which may

also be due to observer artifact, suggests the presence of an expanded trinucleotide repeat in SCA2, as found in SCA1" (page 795, col 2).

Pulst et al. (herein referred to as Pulst) teaches linkage of SCA2 to 12q and established closer flanking markers for SCA2. Pulst teaches that "given the recent identification of an expanded CAG triplet repeat in SCA1, this finding suggests a similar mechanism may underlie at least some case of SCA2 as well" (pages 8, col 2).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art to have modified the method of Trottier for detecting polyglutamine expansion using an antibody with the teachings of Filla or Pulst of the localization of and presence of trinucleotide repeats in SCA2. The ordinary artisan would have recognized the presence of a polyglutamine region within the protein (encoded by a CAG repeat) and would have been motivated to have detected the nucleic acid sequence of the CAG repeat region directly because the direct analysis of the CAG repeat region would allow the ordinary artisan to quantitate the number of CAG repeats within the SCA2 polyglutamine region rather than using the intensity of the signal to estimate the number of repeats. Furthermore, the ordinary artisan would have recognized that the direct detection of a nucleic acid CAG repeat region within the localized nucleic acid would have facilitated a more precise measurement of the number of CAG repeats compared with a qualitative measurement.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the

Art Unit: 1634

unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

12. Claims 27-41 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 1-4 of U.S. Patent No. 6,673,535.

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by or would have been obvious over, the reference claim(s). See e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

Although the conflicting claims are not identical, they are not patentable distinct from each other because Claims 27-41 of the instant application is generic to all that is recited in Claims 1-4 of U.S. Patent No. 6,673,535. That is, Claims 1-4 of U.S. Patent

Art Unit: 1634

No. 6,673,535, fall entirely within the scope of Claim 27-41, or in other words, Claim 27-41 are anticipated by Claims 1-4 of U.S. Patent No. 6,673,535. Here, claim Claims 1-4 of U.S. Patent No. 6,673,535 recites a method for determining whether a human is negative for SCA2 by amplifying using two primers wherein 22 CAG repeats would be negative for SCA2. It is noted 22 CAG repeats is within the range of "normal" and 15-24. The claims are also drawn to detecting SEQ ID NO: 1. Each of the instant claims are within the scope of the patented claims. It is noted that SEQ ID NO: 1 is the genomic DNA for SCA2 and SEQ ID NO: 2 is the cDNA for SCA2. However each of the recited sequences are within the coding cDNA. Thus, Claims 1-4 of U.S. Patent No. 6,673,535 teaches every limitation of the instant claims.

Conclusion

13. No claims allowable.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (571) 272-0743. The examiner can normally be reached Monday-Friday from 7:00 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571) 272-0735.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

The Central Fax Number for official correspondence is (571) 273-8300.

Art Unit: 1634

A handwritten signature in black ink, appearing to read "J. Goldberg". The signature is written in a cursive, flowing style.

Jeanine Goldberg

Primary Examiner

April 13, 2006